

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-61 are pending in the application. Claims 6-8, 10-15, 17, 18 and 20-60 have been withdrawn. Claim 1 has been amended. Support for the amendment to claim 1 can be found, *inter alia*, at paragraph 0017 on page 7, paragraph 0042 on page 15, paragraph 0097 on page 34, and Tables 4 and 5. Claim 61 has been added. Support for new claim 61 can be found, *inter alia*, at page 23, paragraph [0064], and page 25, paragraph [0067].

In the specification, paragraph [0017] and the description of Table 1 on page 19 have been amended to add a SEQ ID NO and remove a hyperlink, respectively.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Objection to the Oath/Declaration***

The Oath/Declaration was objected to as not referring to the preliminary amendment filed March 26, 2004. Paper No. 05192005, page 3. In addition, the amendment filed March 26, 2004 has been objected to under 35 U.S.C. 132(a). In compliance with 37 C.F.R. § 1.67(a), Applicants submit herewith a new Oath/Declaration that refers to the preliminary amendment filed March 26, 2004. Applicants also note that an Application Data Sheet in compliance with 37 C.F.R. §1.76 has been submitted, which contains a reference to Provisional Application No. 60/457,896. Applicants respectfully request withdrawal of these objections.

***Objection to the Specification***

The specification was objected to under 37 C.F.R. 1.821(d) because the specification does not "list the appropriate SEQ ID NO for sequences disclosed in the specification (for example, page 70 at [0205], line 3 and on page 71 at [0206], line 3, both for the nucleic acid sequence GTAAGT)." Paper No. 05192005, page 2. Applicants respectfully submit that 37 C.F.R. 1.821(a) includes in its definition of nucleotide sequences only those sequences that are "an unbranched sequence of ten or more nucleotides." GTAAGT is only six nucleotides in length. Thus, the nucleotide sequence GTAAGT, found at pages 70 and 71, is exempt from the requirements of 37 C.F.R. 1.821(d). Applicants respectfully request reconsideration of the objection in view of the above.

The Examiner objected to the specification because it contains an embedded hyperlink on page 19. Paper No. 05192005, page 3. Applicants have amended the specification to remove the hyperlink. Applicants believe the objection is now moot.

***Rejections under 35 U.S.C. § 112 -- Written Description***

Claims 1-5, 9, 16 and 19 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description support. Paper No. 05192005, pages 4-5. Specifically, the Office Action alleged that the claims encompass a diverse genus of MHC Class I  $\alpha 3$  fragments and/or  $\beta 2$  microglobulin fragments and/or fragments of an antibody specific for a cell surface marker that is not supported by the specification. Applicants traverse this rejection as it may apply to the amended claims.

The Office Action stated that:

The instant claims encompass a composition that comprises fragments of an isolated MHC class I alpha 3 domain and/or a fragment of a  $\beta$ 2m molecule and/or a fragment of an antibody specific for a cell surface marker, including those recited in the instant claims, said fragments not having functional activity, such as binding CD8 and/or  $\beta$ 2m in the case of MHC class I alpha 3 domain fragments,  $\beta$ 2m fragments that don't bind MHC class I molecules effectively or at all, and antibody fragments that do not bind antigen.

Paper No. 05192005, page 4.

Applicants have amended the claims to specify that the fragments have functional activity. Thus, the claims no longer encompass compositions with non-functional fragments.

In addition, the specification as filed discloses relevant identifying structural characteristics of a representative number of fragments within the scope of the invention. For example, at paragraph [0026] on page 10, the specification teaches that mutations at two specific amino acid positions of the MHC class I  $\alpha$ 3 domain are within the scope of the invention. At paragraph [0027] on pages 10-11, the specification teaches a mutation of  $\beta$ 2-microglobulin which is within the scope of the invention. Finally, the specification teaches the antibody fragments Fab, F(ab')<sub>2</sub>, Fv and scFv (acknowledged by Examiner on page 4 of the Office Action), and also teaches immunoglobulin fragments at paragraph [0072] on page 26.

Applicants believe that a representative number of embodiments have been sufficiently described to satisfy the written description requirement. Accordingly, withdrawal of this rejection is respectfully requested.

***Rejections under 35 U.S.C. § 112 -- Incorporation of essential material***

Claims 1-5, 9, 16 and 19 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly incorporating essential material in the specification. Paper No. 05192005, page 5. Specifically, the rejection states that the specification does not include a description of the fragment of complete human HLA-A \*0201  $\alpha$  chain sequence taught by Fayen *et al.*

Applicants have amended the specification to clarify that the sequence taught by Fayen *et al.* is the same as SEQ ID NO:1. Accordingly, Applicants respectfully request reconsideration of this rejection.

***Rejections under 35 U.S.C. § 112 -- Enablement***

At page 6 of the Office Action, claims 1-5, 9, 16 and 19 were rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Specifically, the Office Action states that the scope of the claims would encompass a composition that comprises fragments not having functional activity.

Applicants respectfully disagree with this rejection. "The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art". M.P.E.P. 2164.08(b) Inoperative Subject Matter.

Nonetheless, Applicants have amended the claims to specify that the fragments contained in the claimed composition have functional activity. Thus, the scope of the claims would encompass only operable embodiments.

Additionally, as disclosed in the specification beginning at paragraph [0118] on page 44, the ability of a compound of the present invention to modulate an immune response can be readily assayed. For example, the ability of compounds of the present invention to modulate T cell activity may be determined by measuring IL-2 production (see paragraph [0119] on page 44).

Further, the structural and functional characteristics of a MHC class I  $\alpha 3$  domain,  $\beta 2$  microglobulin molecule, antigenic peptide and antibody specific for a cell surface marker are well known and the specification also describes these characteristics. Modification of these molecules is readily performed and their function readily determined by assay. For example, the specification on page 15 and 16 teaches the modification and production of the MHC class I  $\alpha 3$  domain and  $\beta 2$  microglobulin. At paragraph [0050], methods for determining whether a particular peptide will bind to a particular MHC molecule are discussed. Further, on page 81, Example 6 details an *in vitro* assay for tumoricidal activity of T cells specifically targeted to tumors by compounds of the invention.

Thus, Applicants respectfully assert that one of ordinary skill in the art would be able to make and use the invention, as presently claimed, without undue experimentation. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

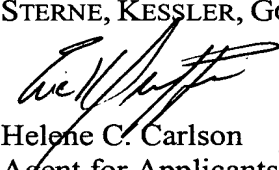
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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